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09/815,944	03/22/2001	Keith D. Allen	R-654	8251

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John E. Burke Esq.
GREENBERG TRAURIG LLP
1200 Seventeenth Street Suite 2400
Denver, CO 80202

EXAMINER

QIAN, CELINE X

ART UNIT PAPER NUMBER

1636

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/815,944

Applicant(s)

ALLEN ET AL.

Examiner

Celine X. Qian Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30 and 32-39 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 30 and 32-39 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 22 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 30, 32-39 are pending in the application.

This Office Action is in response to the Amendment filed on 7/28/05.

Response to Amendment

The rejection of claims 30, 32-39 under 35 U.S.C.101/112 1st paragraph is maintained for reasons set forth of the record mailed on 4/28/05 and further discussed below.

The rejection of claims 30, 32-39 under 35 U.S.C. 112 2nd paragraph is maintained for reasons set forth of the record mailed on 4/28/05 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 30, 32-39 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility.

Claims 30, 32-39 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In response to this rejection, Applicant asserts that the claims are drawn to a transgenic mouse having a disrupted melanocyte stimulating hormone receptor gene and a transgenic mouse whose genome comprises a null allele which comprises polynucleotide encoding a selection

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marker. Applicant argues that the claimed invention has patentable utility according to utility guidelines set forth in MPEP because the claimed invention has a well-established utility.

Applicant assert that the skilled in the art would immediately appreciate how to use a knockout mouse because any knockout mouse has the inherent and well-established utility of defining the function and role of the disrupted gene regardless of specific phenotypes, characterizations or properties of the knockout mouse. Further, Applicant asserts that studying the function of the melanocyte stimulating hormone receptor is a substantial utility because there is no further research required to confirm the utility of the claimed mouse in determining melanocyte stimulating hormone receptor function because 1) the value of the knockout mouse is well established in the art; 2) further characterization of the mouse itself is not required to confirm its utility in studying the melanocyte stimulating hormone receptor function; 3) Applicant has provided an *in vivo* model for studying the function of the melanocyte stimulating hormone receptor gene which is associated with hypoactivity. Applicant indicates that the claimed invention is purchased by two large pharmaceutical company and database comprising tests of the mouse has been subscribed by three pharmaceutical companies, thus such commercial acceptance more than satisfied the practical utility requirement of 101 and 112 1st paragraph according to *Brenner v. Manson* and *Phillips Petroleum Co. v. U.S. Steel Corp.*, and *Lipscomb's Walker on Patents* 5:17, p 562 (utility may be evidenced by sales and commercial demand). Applicant asserts that Pillips applies to the instant case because the pharmaceutical company's use of the mouse would infringe the claims if the patent is issued. Moreover, Applicants assert that the utility to study melanocyte stimulating hormone receptor gene function and expression using the claimed mouse is specific to the melanocyte stimulating hormone receptor gene

knockout mouse because no other mouse can be used for this purpose. Applicant thus concludes that the claimed invention has credible, substantial and specific utility which satisfies the statute of 35 U.S.C. 101, and enabled by the instant specification.

These arguments have been fully considered but deemed unpersuasive. The reasons for the utility and non-enablement rejection were discussed in detail in the office action mailed on 4/28/05 and in the utility rejection discussed above. In response to Applicant's response regarding any knockout mouse has a well-established utility, the examiner does not agree with Applicant's assertion that the claimed invention has a well-established utility. Applicant is reminded that in MPEP, the guideline for the utility requirement clearly states: "An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible." In the instant case, the utility that applies to any knockout mouse is not specific to the claimed invention, the melanocyte stimulating hormone receptor transgenic mouse having a null allele that comprises exogenous DNA. It was well known to knock out a gene to determine its function or what will happen when the gene is not expressed. However, scientific "utility" is not the same as "patentable utility" or a "well-established" utility, of which must be specific, substantial and credible. At the time of filing, knockout mice were used for further research in the art as indicated by the quotations cited by Applicant, for example, studying gene function. However, further research does not rise to the level of a "well-established utility" because such a utility is not substantial. The utility

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guidelines specifically state that further research is not a "substantial utility." The MPEP states "the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities": A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved..." In the instant case, further study of mice would have been required to determine how to use the mouse of applicant's invention according to the embodiments described in the specification since the overall phenotype of the claimed mice does not correlate with any disorder; Therefore, further study would be required to characterize such association because the teaching of the specification is not sufficient to establish whether the phenotype is directly result from the gene disruption. Further study would be required to determine the function of the disrupted gene and its role in the resultant phenotype. Furthermore, the overall phenotype of the claimed mice does not correlate to any disorder; therefore, further study would be required to determine how to use the mice to study a disorder, screening drugs and treatment for such disorder. Thus, using the mice claimed for further research is not a "substantial utility."

With regard to the well-established utility of studying gene function as asserted by Applicant, Olsen (GABA in the Nervous System, 2000, pg 81-95) taught that "although gene targeting is often useful in delineating the contribution of a given gene product to phenotypic characteristics observed, some gene knockouts lead to embryonic or perinatal lethality, and others lead to no apparent phenotype. This can arise from a lack of any role for the gene in question in regard to the trait studies or from

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compensation by other gene products. Analysis of the compensation can yield valuable clues to the genetic pathway" (pg 82, last 11 lines of col. 1). As such, a knockout mice may not be capable of elucidating the function of the protein and may only provide a clue to a pathway the protein being knocked out is involved in. Using the claimed mice to obtain a clue to a pathway is not a "substantial utility." Using a mouse with a phenotype caused by genes compensating for a knocked out gene is not a "specific utility" because the phenotype is not specific to the knocked out gene.

In response to Applicant's argument of the commercial sale of the claimed mouse, Applicant is reminded that the sale of a product does not automatically gives the product patentable use according to the statute of 35 U.S.C.101 and the utility guideline set forth in the MPEP. Commercial success is only considered as secondary evidence for overcoming a 103 (a) rejection according to guidelines set by MPEP. *Brenner v. Manson* does not validate the notion that commercial use automatically gives a claimed product patentable utility. The subscription of three company to the Deltabase does not give automatically gives the claimed mouse patentable utility because it is unclear what data the companies are interested and what they are used for. The declaration under 37 CFR 1.132 has been fully considered, however, it is not sufficient to provide a patentable utility and enable the instantly claimed invention. The purchase of the claimed mouse by two large pharmaceutical company neither proves commercial success of the claimed mouse nor does it gives the claimed mouse a patentable utility. The case law of *Phillips Petroleum Co. v. U.S. Steel Corp.* 6 USPQ 2d 1065 talks about commercial success in context as secondary consideration in favor of nonobviousness (see page 1096). It states "of course, there must be a nexus "between the merits of the claimed invention and the

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evidence offered if that evidence is to be given substantial weight enroute to conclusion on the obviousness issue." *Stratoflex* , 713 F.2d at 1539 [218 USPQ at 879] (noting *Solder Removal Co. v. United States Intern. Trade* , 582 F.2d 628, 637 [199 USPQ 129, 137] (C.C.P.A. 1978)).

Crystalline polypropylene is one of the most widely used chemical compositions in commerce today. Worldwide demand is presently approximately fourteen billion pounds, with the United States' demand totaling nearly six billion pounds per year. (Mark, Tr. at 503.) 68 Experts from both sides were in general agreement that crystallinity is the characteristic which gives polypropylene its immense commercial value." According to the case law, the commercial success is established by the worldwide use of the claimed compositions and the generation of high revenue from the sale of the claimed composition. However, the sale of the present claimed invention to two pharmaceutical company clear does not mount to such "commercial success." The case law of 9 USPQ 2d 1461 affirmed the earlier case but does not deal with commercial success and practical utility. It states: "correct finding of infringement of otherwise valid claims mandates as a matter of law a finding of utility under §101," however, it does not apply to the current situation since there is no infringement of the current claimed invention. Applicant's argument with regard to infringement is unpersuasive because infringement would not occur before the issuance of a patent. Nor does infringement decided by Applicant. With regard to the sentence quoted from Lipscomb's Walker on Patents, the examiner cannot comment on it because it is unclear what context such statement was made. For example, what evidence should Applicants provide to establish sales and commercial demand? Is it a secondary evidence to some other requirement? A search of the book reveals that it ends at page 530, there is no page or paragraph 562. As such, this statement alone does not support that sale of this mouse to one

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company automatically gives the claimed mouse a patentable utility. Therefore, based on the utility requirement set forth in MPEP, the sale of the mouse to one company does not give the claimed mouse a patentable utility.

In response to Applicant's argument with regard to specific utility, Applicant is again reminded that the asserted utility of the claimed invention need to be credible, substantial and specific according to the 101 statute. The utility of studying melanocyte stimulating hormone receptor function using the claimed mouse fails to meet this requirement (see reasons given above). As discussed in Crawley et al. (page 108 2nd col., 3rd paragraph), no single behavior commonly measured in the open field reflects only anxiety or emotional reactivity. The open field parameters reflects multiple underlying traits which indicates that genes linked to open field performance may be involved in the regulation of many activities including locomotor, exploratory, olfaction and vision. Thus, further research is required to determine which functional pathway the melanocyte stimulating hormone receptor is involved in. There is no support that from the instant specification that said receptor is directly involved in hypoactivity. Moreover, if the phenotype of the mouse is not directly resulted from the disruption of the gene, the association between the phenotype is not specific to the disruption of the melanocyte stimulating hormone receptor gene. As such, the claimed mouse fails to meet the standard.

In response to Applicant's argument regard using the transgenic mouse comprising null-reporter allele to study the gene expression, Applicant is reminded that studying the expression of a gene of which the function is not known is not a substantial

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utility. Studying the expression of a gene for the purpose of exploiting said gene function is not a substantial utility because further research is required to determine said gene function, and such gene expression pattern merely provides a clue for said gene function. The “clue” does not rise to the level of a substantial utility. Similarly, studying the expression of a gene for the purpose of determine how to use said transgenic mouse constitutes further research to determine how to use the claimed product, thus it does not provide a substantial utility to the claimed product. Therefore, the specification fails to teach a patentable utility for the claimed mouse.

For reasons given in the previous office action and above, the specification fails to disclose a credible, substantial and specific use for the claimed mouse and one skilled in the art would not know how to use the claimed mouse according to the embodiments disclosed by the instant specification. Applicants did not provide additional arguments with regard to the 112 1st paragraph rejection, thus the rejection is maintained for same reasons as set forth in the previous office action and discussed in the utility rejection above. Therefore, the 101/112 1st paragraph rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30, 32-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 30, 32-39, the recitation of “mRNA comprising a polynucleotide sequence of SEQ ID NO:19” renders the claim indefinite because SEQ ID NO:19 is a DNA sequence rather than an RNA sequence.

In response to this rejection, Applicant argues that SEQ ID NO:19 corresponds to X65635 which is mRNA.

This argument is deemed unpersuasive. According to sequence listing submitted with the instant application, the nucleic acid sequence of SEQ ID NO:19 comprises nucleotide “T” rather than “U.” The examiner is unaware of the existence of any mRNA comprises nucleotide “T” in the art.

Regarding claim 30, the recitation of “pseudopregnant mouse gives birth” renders the claim indefinite because a “pseudopregnant mouse” cannot give birth.

In response to this rejection, Applicant argues that the pseudopregnant mouse can give birth to chimeric mice as taught by Biology of Cell (Albert, 4th ed.) such that the terminology would be clearly understood by one skilled in the art.

The argument has been considered but deemed unpersuasive. Applicant is reminded that once the blastocyst is introduced into the pseudopregnant mouse, said mouse is no longer pseudopregnant, but actually pregnant. It is this mouse that gives birth to the chimeric mouse. The teaching of the Biology of Cell also illustrates this process, not just a pseudopregnant mouse that would give birth to a chimeric mouse. Applicant is advised to use language particularly pointing out and distinctly claiming the subject matter. This rejection is thus maintained.

Please note, claims 34 and 35 were canceled in the Amendment filed on 5/23/03 and 3/22/04. The newly introduced claims are different from the original claims 34 and 35. Appropriate numbering is required.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELIAN QIAN
PATENT EXAMINER

